REMARKS

The Official Action of 11 December 2008 has been carefully considered and reconsideration of the application as amended is respectfully requested.

IDS

The Examiner states that JP 5-55148 has not been considered. Applicants' respectfully advise the Examiner that JP 5-55148 is a family member of EP 0419275, an English language reference listed at "AO" of one of the PTO Form 1449 attached to the Official Action. Accordingly, JP 5-55148 is cumulative to information already of record or being made of record in the application.

Specification

The specification is objected to as failing to provide proper antecedent basis for the recitations of viscosity higher than 22,000Pas, and a block copolymer having more than three blocks. These recitations are now deleted from the claims.

Claim Objections

Claim 53 is objected, but was cancelled in a previous correspondence, therefore, this objection is moot.

Claim 63 is objected, but the claim is currently cancelled, therefore, this objection is moot.

Claim 96 is objected to because of a typographical error (DMB instead of DBM). The typographical error is currently corrected. Claim 86 is similarly corrected.

Claim rejections – 35 USC § 112

Claim 51 and its dependent claims are rejected for reciting the term "the polymer system" without antecedent basis. Claim 51 is currently amended to recite a polymeric system to provide the requisite antecedent basis.

Claim 82 is rejected for reciting both broad limitations (RTG polymer) and a narrow limitation (specific polymers). This claim is currently amended to recite only the broad limitation.

Claims 84, 94, 86, 96, 87, 97, 98, and 89 are rejected for reciting both broad and narrow limitations. These claims are currently amended to recite only the broad limitations. Claim 92 is similarly amended. The narrower limitations are recited in new claims 106 to 116, 121 and 122.

Claims 90-92 are rejected for reciting "said responsive polymeric system" without antecedent basis. Claim 88, on which the rejected claims depend is currently amended to include the term "responsive polymeric system" to provide the requisite antecedent basis.

Claim Rejections – 35 USC § 103

Scarborough and Cohn

Claims 51, 52, 55-58, 63, 67, 81-90 and 92-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scarborough (US 2002/0132012) in view of Cohn et al (2003; J. Mat. Sci).

Cohn et al was published in February 2003, which is after the priority date (September 4, 2002) of Applicants' priority application, PCT/IL02/00736, which was filed in English. Therefore, Cohn et al is not citable as prior art against the subject claims (see MPEP 201.15). In any event, this rejection is based on Scarborough as the primary reference and Cohn cannot supplement the deficiencies in Scarborough which are discussed below.

Scarborough, Bentley, and Maeda

Claims 51, 52, 55-58, 63, 67, 81, and 83-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scarborough (US 2002/0132012) in view of Bentley et al (US 2006/0239961, hereinafter Bentley) in further view of Maeda et al. (1998; J. Appl. Poly. Sci, hereinafter Maeda). The applicants respectfully traverse.

The independent claims

Of the claims under consideration in the Official Action, only claims 51 and 88 are independent.

Independent claim 88 is not addressed in the rejection other than by its inclusion in the list of rejected claims at the heading of the rejection, on page 6. If the claim is rejected in the next Office Action, the applicants respectfully request explicit explanations as to the grounds of the rejection, and making the next Office Action non-final, as it will be the first Action in which a rejection to this independent claim is explained.

The above 103 rejection is based on the Office contention that "Scarborough teaches a composition comprising bone marrow cells (BMC), demineralized bone matrix (DBM) ... and reverse phase block copolymers". The applicants traverse; and submit that Scarborough does not teach such a composition.

Scarborough teaches a flowable bone composition comprising bone component and a carrier. The composition may be combined with medically useful substances. While Scarborugh describes a genus that may encompass the aforementioned composition, this by itself is insufficient to render the aforementioned combination obvious.

In more detail, Scarbourough describes each of the above components of the flowable bone compositions as follows:

The Bone Component

"The bone component may be mineralized, partially demineralized or demineralized as well as combinations thereof "(paragraph [0014]).

The Carrier

"Suitable carriers can be any of a number of compounds and/or polymers, e.g.,

1. polymer sugars,
2. proteins,
3. long chain hydrophilic block copolymers,
4. reverse phase block copolymers,
5. hyaluronic acid,
6. polyuronic acid,
7. mucopolysaccharide,
8. proteoglycan,
9. polyoxyethylene,
10. surfactants, e.g., the pluronics series of nonionic surfactants, and
11. peptide thickener.

Suggested classes of biocompatible fluid carrier would include polyhydroxy compound, polyhydroxy ester, fatty alcohol, fatty alcohol ester, fatty acid, fatty acid ester, liquid silicone, mixtures thereof, and the like" (paragraph [0020], indentation and numbering added).

The Medically Useful Substances

"Medically/surgically useful substances, which can be readily combined with the bone component, fluid carrier and/or osteoinductive composition of this invention, include, e.g.,

1. demineralized bone powder as described in U.S. Pat. No. 5,073,373 the contents of which are incorporated herein by reference,
2. all collagen types (not just type I),
3. insoluble collagen derivatives,
4. non-collagenous proteins such as osteopontin, osteonectin, bone sialo proteins, vitronectin, thrombospondin, proteoglycans, decorin, biglycan, aggrecan, veriscan, tenascin, matrix gla protein hyaluronan; hydroxyapatite, etc., and
5. soluble solids and/or liquids dissolved therein, e.g., antiviricides, particularly those effective against HIV and hepatitis; antimicrobials and/or antibiotics such as erythromycin, bacitracin, neomycin, penicillin, polymyxin B, tetracyclines, viomycin, chloromycetin and streptomycins, cefazolin, ampicillin, azactam, tobramycin, clindamycin and gentamycin, etc.;
6. amino acids,
7. peptides,
8. vitamins,
9. inorganic elements,
10. inorganic compounds,
11. cofactors for protein synthesis,
12. hormones;
13. soluble and insoluble components of the immune system,
14. soluble and insoluble receptors including truncated forms,
15. soluble, insoluble and cell surface bound ligands including truncated forms; chemokines,
16. bioactive compounds that are endocytosed;
17. endocrine tissue or tissue fragments;
18. synthesizers;
19. enzymes such as collagenase, peptidases, oxidases, etc.;
20. polymer cell scaffolds with paraenchymal cells;
21. angiogenic drugs and polymeric carriers containing such drugs;
22. collagen lattices;

23. biocompatible surface active agents;
24. antigenic agents;
25. cytoskeletal agents;
26. cartilage fragments,
27. living cells such as chondrocytes, bone marrow cells, mesenchymal stem cells,
28. natural extracts,
29. tissue transplants,
30. bioadhesives,
31. bone morphogenic proteins (BMPs), transforming growth factor (TGF-beta), insulin-like growth factor (IGF-1) (IGF-2), platelet derived growth factor (PDGF), fibroblast growth factors (FGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF),
32. angiogenic agents,
33. bone promoters,
34. cytokines,
35. interleukins,
36. genetic material, genes encoding bone promoting action, cells containing genes encoding bone promoting action;
37. hormones,
38. growth hormones such as somatotropin;
39. bone digestors;
40. antitumor agents;
41. fibronectin;
42. cellular attractants and attachment agents;
43. immuno-suppressants;
44. bone resportion inhibitors and stimulators;
45. angiogenic and mitogenic factors;
46. bioactive factors that inhibit and stimulate second messenger molecules;
47. cell-matrix and cell-cell adhesion molecules;

48. clotting factors;
49. externally expanded autograft or xenograft cells,
50. permeation enhancers, e.g., fatty acid esters such as laureate, myristate and stearate monesters of polyethylene glycol, enamine derivatives, α-keto aldehydes, etc.; and,
51. nucleic acids and any combination thereof." (Paragraph [0017], indentation and numbering added).

Thus, the composition allegedly taught by Scarborough may be found in the reference only if one cherry-picks the third out of three possibilities suggested for bone material, the fourth out of 10 possibilities suggested for carriers and second example provided for the 27th out of 51 possibilities suggested for medically/surgically useful agents. Even in the most conservative approach, Scarborough describes a genus of more than 1500 species, and includes no teaching or suggestion whatsoever to pick the one that the Office Action states it teaches. Scarborough does not provide any example for a composition comprising bone marrow cells (BMC), neither for a composition comprising reverse phase block copolymer. The only example of a composition in Scarboruogh (Example I, paragraphs [0032] and [0033]) is for a composition of DBM in glycerol.

The applicants respectfully note that a publication teaches a combination only if one of ordinary skill in the art is able to "at once envisage" the specific combination. (see MPEP 2131.02 discussing anticipation of a species by disclosure of a genus).

Furthermore, MPEP 2144.08, discussing (non)obviousness of a species over a disclosure of a genus, explicitly states that "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness".

The Office Action does not contain any underpinning rationale why would it be obvious for a person of ordinary skill to practice the combination of DBM, BMC and reverse phase polymers out of the many hundreds of alternatives provided by Scarborough.

Thus, not only that Scarborough does not *teach* "a composition comprising bone marrow cells (BMC), demineralized bone matrix (DBM) ... and reverse phase block copolymers" as alleged by the Office, but it does not even render such a combination obvious. At least for this reason, the Office Action does not set forth a *prima facie* case of obviousness against the independent claims.

Furthermore, claim 51 contains a feature that the polymer is "capable of undergoing a condensation reaction in the presence of water resulting in an increase in the molecular weight of the polymeric system". The Office Action acknowledges that the cited combination is silent regarding this feature, but asserts that "since the copolymer of Bentley et al is considered substantially similar, if not identical to the claimed copolymer, it is expected that the poly(ether carbonate) of Bentley et al. would have the identical property as the claimed copolymer.

The Examiner generously adds that "clear evidence that the copolymer of the cited prior art do not possess a critical characteristic that is possessed by the claimed copolymer, would advance prosecution and might permit allowance of claims to applicants' copolymer".

The applicants respectfully submit that they do not claim any polymer per se. However, the polymer recited in the claims has the aforementioned feature of being "capable of undergoing a condensation reaction in the presence of water resulting in an increase in the molecular weight of the polymeric system", while Bentley's polymers do not have this feature.

Bentley supplies clear evidence that his polymers do not have the aforementioned feature. In fact, Bentley teaches that his polymers undergo, in the presence of water, a reaction resulting in *decrease* of the molecular weight. The opposite effect to that recited in claim 51.

In particular, Bentley states, on paragraph [0024] as follows:

> "The polymers of the invention, by virtue of their carbonate linkages, are hydrolytically degradable under mild conditions, and hydrolyze to produce soluble oligomer fragments, of significantly lower molecular weight that the starting polymer."

Thus, Bentley is not silent regarding the aforementioned feature, but rather teaches the opposite.

In summary, the applicants contend that Scarborough does not teach or suggest a composition comprising bone marrow cells (BMC), demineralized bone matrix (DBM) and reverse phase block copolymers, and therefore, the Office Action fails to establish a *prima facie* case of obviousness against any of the claims under consideration.

Furthermore, neither Scarborough nor Bentley describes a polymeric system having the aforementioned feature, and this is an additional reason for which the Office Action fails to establish a *prima facie* case of obviousness against claim 51.

The dependent claims

All the dependent claims are patentable at least for the virtue of being dependent on a patentable base claim. Nevertheless, Applicants briefly discuss the patentability of some of the dependent claims independently of the patentability of the base claims:

Claims 89, 118, 119, and 120

Claim 89 contains a feature that the "site-responsive polymer is a polymeric system or RTG polymer comprising at least one silicon-containing reactive group". New claim 118 also recites at least one silicon-containing reactive group. The Office Action states, on page 12, as follows: "with regard to the limitation of claim 89 drawn to the polymer having silicon-containing reactive group, Scarborough teaches that liquid silicone such as polymethyl siloxane and poly(dimethyl siloxane) and polyalky arylsiloxane can be a carrier for the composition comprising BMC and DBM (para. 20 and 26)".

The applicants respectfully submit that the silicones suggested by Scarborough do not contain any silicon-containing ***reactive*** groups. No person of ordinary skill in the art would consider the silicon-containing groups in theses silicones to be reactive.

New claims 119 and 120 recite that the "silicon-containing reactive group reacts at 37°C to increase the molecular weight of the polymeric system". The silicon-containing groups of Scarborough's liquid, to which the Examiner refers, certainly are incapable of reacting at this temperature.

Independent Claims 123 and 124

New independent claim 123 corresponds to claim 51 with an exception that it does not recite the viscosity increase recited in claim 51. The viscosity increase is not required

in order to distinguish the claims from the cited art and the claim is patentable for the reasons discussed above with respect to Claim 51. Claim 124 corresponds to claim 51, but is narrower in that the viscosity increase is recited to be a result of the condensation reaction. Thus claim 124 is patentable at least for the same reasons explained with regard to claim 51.

In view of the above, Applicants respectfully submit that the prior art rejections and all other rejections and objections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

CLIFFORD J. MASS
LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NEW YORK 10023
REG. NO. 30086 (212)708-1890